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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,952	03/10/2004	Matthew Oliver Fraser	046562/274659	4482

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,952	FRASER ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-40 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 09/21/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species "overactive bladder" without traverse within the group of urinary tract disorders, "orally" with traverse within in the group of methods of administration, "ziconotide" with traverse within the group of Cav2.2 calcium channel modulators and "ω-conotoxin" without traverse within the group of second Cav2.2 calcium channel modulators in the reply filed on November 3, 2004 is acknowledged.

Applicant's election with traverse of method of administration of the drug 'orally' and the election of the species 'ziconotide' within the group of Cav2.2 calcium channel modulator with traverse in the reply filed on November 3, 2005 is acknowledged. The traversal is on the ground(s) that the invention comprises the use of a combination of Cav2.2 calcium channel modulator compounds used in the treatment of lower urinary tract disorders and that the search and examination of the application is not burdensome. It's the applicant's argument that the Examiner must examine the application in its entirety on the merits even though the application includes claims that embody independent and distinct inventions. This is not found persuasive because the compounds of the instant application are distinct, absent evidence to the contrary, and would require a unique search strategy. The search for the distinct compounds is conducted based on their chemical structure. Therefore, the search of one chemical structure would not necessarily lead to the discovery of another structure, nor would it necessarily lead to the discovery of methods of using and/or making. The search for each of the above inventions is not co-extensive particularly with regard to the non-patented literature search. Further, a reference that would anticipate the invention of one group would not necessarily anticipate or even make

obvious another group. Because these inventions are distinct for the reasons given above, the search for one invention would not necessarily lead to the discovery of another invention, restriction for examination purposes as indicated is proper, and not to restrict would be an undue burden on the Examiner.

Examiner required an election of species on the claims submitted with the application. Upon election of species, if the elected species is free of prior art, then more species will be searched. However, the Examiner has agreed and accepted to consider and to work on conotoxin and ziconotide in view of applicant's argument.

The restriction requirement is still deemed proper and is therefore made FINAL.

It is hereby brought to the attention of the applicant that the election of the species "ziconotide" has been referred to as category "l" of claim 33 (page 3, paragraph 2 of the facsimile dated November 2, 2004). However, the species "ziconotide" has been referred to as category "m" of claim 33.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maggi, et al., (Naunyn-Schmeiedeberg's Arch Pharmacol, 1988, 338, 107-113), in view of Yoshimura, et al., (J. Neurophys., 2001, 86, 304-311).

Applicants claim a method of treating a lower urinary tract disorder by administering to an individual a calcium channel modulator. In the instant case applicants have elected ω-conotoxin GVIA and the synthetic equivalent ziconotide as the calcium channel modulator to treat overactive bladder symptom by administering the medication orally.

Maggi, et al., teaches the use of ω-conotoxin to study the effect of the ω-conotoxin on the neuronal calcium channels in rat and guinea pig urinary bladder. Maggi, et al., found that the ω-conotoxin produced a concentration and time dependent inhibition response to twitches stimulated by applied electrical field in rat and guinea pig urinary bladder at 100 fold lower concentration compared to tetrodotoxin (page 108, column 2). They found that ω-conotoxin was effective at 1 nM compared to 0.5 μM of tetrodotoxin. They also found that with increase in the concentration of the ω-conotoxin, the time required for inhibitory response was more rapid and was evident within 2-4 minutes at 0.1-1.0 μM compared to 1 h at 1 nM concentration.

Nitric oxide (NO) has been known to be a signal transmitter at various sites in the neural pathways controlling the urogenital organs. Yoshimura, et al., have studied the effect of NO on the dorsal root ganglion (DRG) neurons innervating the urinary bladder by looking at the high

voltage calcium channel currents in whole cells isolated from urinary bladder of rats. Oral administration of NO precursor such as L-arginine was effective in reducing irritable bladder syndrome (page 310,, column 2). It has been demonstrated that NO acts on the same Ca^{2+} channel as ω-conotoxin (page 308, column 1; abstract). It is also known that NO exerts multiple actions on various types of voltage-sensitive ion channel through cGMP dependent and/or cGMP independent mechanisms (page 308, column 2). Yoshimura, et al., have established a well-accepted model to measure calcium channel currents in urinary tract disorders involving bladder sensory nerves. Yoshimura, et al., have shown that ω-conotoxin GVIA is effective in reducing 90% of high voltage activated Ca^{2+} channel current in the presence of a NO donor such as S-nitroso-N-acetylpenicillamine (SNAP) (Page 308 column 1).

The compound ω-conotoxin is well known in the literature extracted from the venom of fish hunting marine snail. Maggi, et al., have shown the use of the ω-conotoxin to study effect of the ω-conotoxin on the neuronal calcium channels in rat and guinea pig urinary bladder. The study of Maggi, et al., indicated that ω-conotoxin is 100 fold more effective in suppressing the motor sensory responses of urinary bladder under the influence of an applied electrical potential. Yoshimura, et al., describes the model system to study the effect of ω-conotoxin on the neurons innervating the urinary bladder. In addition to this, NO acts on the same Ca^{2+} channels as ω-conotoxin and NO has other types of activities such as cGMP dependent and/or independent activities (page 308, column 2). Therefore, it is obvious to use ω-conotoxin instead of NO or NO precursors in order to obtain the desired effect of blockage of Ca2+ channels for treatment of bladder, without the other undesired effects of NO. In the present instance the applicant's method of treating the urinary tract disorder dwells on the teachings of Maggi, et al., and Yoshimura, et

al. Therefore, there would have been reasonable expectation of success to combine the teachings of Maggi and Yoshimura to arrive at the method proposed by the applicants to treat the lower urinary tract disorder. Therefore, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

INFORMATION DISCLOSURE STATEMENT (IDS)

Some references were not considered because a copy of the reference was not supplied.

Conclusion

ALL CLAIMS ARE REJECTED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

srg

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SUPERVISORY PATENT EXAMINER
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